Conclusions: The aforementioned clinical outcomes and comparative analysis is essential for furthering our understanding of the factors which influence patient outcomes in the treatment of cartilage injury by autologous chondrocyte implantation therapy such as MACI.

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EARLY REDUCTION IN ULCER COMPLICATIONS WITH LUMIRACOXIB COMPARED WITH NSAIDS: DATA FROM TARGET

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Purpose: A 79% reduction in upper gastrointestinal (GI) ulcer complications has been reported for lumiracoxib compared with nonsteroidal anti-inflammatory drugs (NSAIDs) (naproxen or ibuprofen) over 52 weeks in the non-aspirin population of the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET). However, guidelines indicate that these agents should be used for the shortest possible duration. We investigated how early after the start of treatment a significant benefit of lumiracoxib could be detected in TARGET.
Methods: TARGET randomized 18 325 patients >50 years of age with osteoarthritis (OA) to receive lumiracoxib 400 mg once daily (4x the recommended dose for OA) vs ibuprofen 800 mg three times daily or naproxen 500 mg twice daily for 52 weeks in one of two sub-studies. Randomization was stratified for age and low-dose aspirin use. The primary analysis population included patients not taking low-dose aspirin, comprising n=6950 patients treated with lumiracoxib and n=6968 with NSAIDs (naproxen, n=3537; ibuprofen, n=3431). The primary endpoint was the cumulative incidence of blindly and independently adjudicated definite or probable upper GI ulcer complications. The secondary endpoint was the incidence of definite or probable upper GI ulcer complications and symptomatic ulcers (all ulcers). In these analyses, pointwise 95% confidence intervals (CI) were generated for the between-treatment differences in Kaplan-Meier estimates (KMEs) for all ulcers and ulcer complications in the non-aspirin population.
Results: Based on the upper 95% CIs for the difference in Kaplan-Meier estimates, in the non-aspirin population there was a significant reduction in all ulcers by Day 8 with lumiracoxib compared with NSAIDs. For ulcer complications, a significant reduction with lumiracoxib compared with NSAIDs occurred by Day 16. When analyzed by sub-study, the advantage of lumiracoxib on all ulcers occurred as early as by Day 6 versus naproxen (Figure 1) and by Day 32 versus ibuprofen. For ulcer complications, a significant reduction was seen with lumiracoxib by Day 14 versus naproxen and Day 33 versus ibuprofen.

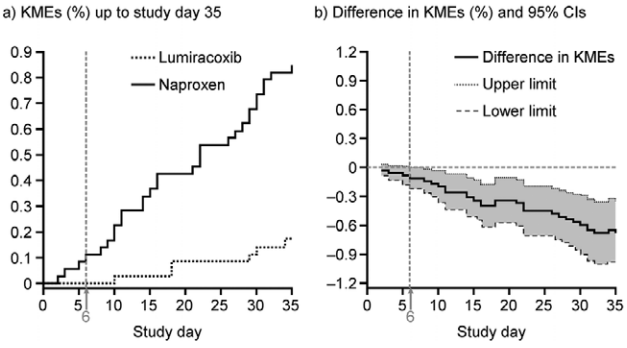

Figure 1

Conclusions: The long-term GI benefit of lumiracoxib compared with traditional NSAIDs has been demonstrated previously. However, even when given for short periods, the selective COX-2 inhibitor lumiracoxib appears to have significant GI safety advantages over nonselective NSAIDs.

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COMPARISON OF EFFICACY OF LUMIRACOXIB WITH CELECOXIB AND PLACEBO IN KNEE OSTEOARTHRITIS PATIENTS AND DIFFERING BASELINE DISEASE SEVERITY

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Purpose: To evaluate if the efficacy of lumiracoxib 100 mg od and celecoxib 200 mg od differed in patients with knee osteoarthritis (OA) as a function of baseline disease severity.
Methods: Data from two 13-week, multicenter, randomized, double-blind, double-dummy, placebo-controlled studies comparing lumiracoxib 100 mg od with celecoxib 200 mg od and placebo were combined for efficacy analysis based on baseline disease severity. The co-primary endpoints included assessment of OA pain intensity in the target knee (VAS), patient's global assessment of disease activity (VAS) and WOMAC™ LK3.1 total score at study end. Disease severity at baseline was defined as high, medium, or low using the median of the baseline values for each of the three primary assessments. A patient was classified with high baseline disease severity if all 3 baseline values were greater than their respective median, medium baseline disease severity if 1 or 2 baseline values were greater than their median and low baseline disease severity if none of the 3 baseline

Abstract 260 – Table 1. Efficacy of lumiracoxib in the disease severity subgroups at 13 week

Efficacy variable	Pair wise Comparison	High severity group		Medium severity group		Low severity group	
		Estimated difference (95% CI of difference)	P-value	Estimated difference (95% CI of difference)	P-value	Estimated difference (95% CI of difference)	P-value
OA pain	Lumiracoxib *vs* placebo	-9.30 (-13.25,-5.34)	<0.001	-5.48 (-8.41,-2.55)	<0.001	-4.74 (-8.44,-1.03)	0.012
	Celecoxib *vs* placebo	-6.70 (-11.22,-2.19)	0.004	-4.76 (-8.15,-1.38)	0.006	-4.74 (-9.03,-0.45)	0.030
	Lumiracoxib *vs* celecoxib	-2.59 (-6.44,1.25)	0.186	-0.71 (-3.67,2.24)	0.636	0.00 (-3.70,3.71)	0.998
Patient's global assessment of disease activity	Lumiracoxib *vs* placebo	-9.83 (-13.74,-5.93)	<0.001	-8.09 (-10.99,-5.20)	<0.001	-4.21 (-7.87,-0.55)	0.024
	Celecoxib *vs* placebo	-6.63 (-11.09,-2.18)	0.004	-6.10 (-9.45,-2.75)	<0.001	-3.47 (-7.72,0.77)	0.109
	Lumiracoxib *vs* celecoxib	-3.20 (-7.00,0.60)	0.099	-1.99 (-4.91,0.93)	0.181	-0.74 (-4.40,2.93)	0.694
WOMAC™ total score	Lumiracoxib *vs* placebo	-8.08 (-10.86,-5.30)	<0.001	-5.26 (-7.32, -3.19)	<0.001	-4.11 (-6.72,-1.50)	0.002
	Celecoxib *vs* placebo	-5.62 (-8.79,-2.44)	<0.001	-4.94 (-7.32,-2.56)	<0.001	-3.24 (-6.26,-0.22)	0.036
	Lumiracoxib *vs* celecoxib	-2.47 (-5.17,0.24)	0.074	-0.32 (-2.40,1.77)	0.767	-0.87 (-3.48,1.74)	0.513